REMARKS

Claims 1-32 are pending. Claims 1, 11, 17 and 27 have been amended to introduce certain format changes. Applicants submit that these amendments raise no issue of new matter. Thus, claims 1-32 will remain pending and under examination upon entry of this amendment.

In view of the arguments set forth below, applicants maintain that the Examiner's rejections made in the January 16, 2004 Final Office Action have been overcome, and respectfully request that the Examiner reconsider and withdraw same.

Rejections Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 1-32 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to allow one skilled in the relevant art to which it pertains to make and/or use the invention commensurate in scope with the claims.

Applicants understand this rejection to be based upon the Examiner's assertion that one of skill in the art would not expect the antigen presenting cells (APCs) of the claimed method to stimulate a TH-1 response in view of Grufman (2000), La Sala (2001), and La Sala (2002), and therefore undue experimentation is required to practice the claimed methods.

In response, applicants respectfully traverse for the reasons of record and for the additional reasons set forth below.

The pending claims are directed to a method for priming APC cells which comprises contacting the APC cells with a ligand-coated antigen/ATP-filled particle under conditions permitting the phagocytosis of the particle by the APCs.

Grufman teaches that IL-12 is required for a cytotoxic T-cell (TH-1) response. Notably, Grufman does not teach the claimed method of

priming APCs. In Grufman, dendritic cells are simply incubated with a peptide antigen in culture media (see page 1092, column 1).

La Sala (2001 & 2002) teaches that micromolar amounts of *extracellular* ATP induce dendritic cells to acquire properties of mature cells which exhibit a reduced capacity to produce IL-12 and induce a TH-1 response.

Importantly, the APCs of the instant methods ars not exposed to increased *extracellular* ATP. Rather, the concentration of ATP *within* the cell is increased following phagocytosis of the Ag/ATP-filled particle. There is nothing in La Sala to suggest that increased *intracellular* ATP would alter the dendritic cells in a manner that reduces their capacity to induce a TH-1 response. Thus, contrary to the Examiner's assertion, there is no suggestion in the cited references that applicants' method would fail to produce APCs capable of inducing a TH-1 response *in vivo*. Moreover, applicants' working example demonstrates that the claimed method induces CD8+ T-cell proliferation better than priming with peptide alone (e.g., the method used in Grufman). Thus, the specification provides an example demonstrating that applicants' method is a significant improvement over the prior art of priming APC cells.

Applicants understand the Examiner's remarks regarding the alleged unpredictability in the art to have been based on the Examiner's mistaken assumption that applicants' method comprised exposing APCs to at least micromolar concentrations of *extracellular* ATP. Accordingly, this position is inapposite to the claimed method in view of the fact that the instant method does not involve exposing APCs to increased extracellular ATP. Applicants nevertheless make the following additional remarks in order to underscore their position.

As taught in the specification at pages 2-3, and at page 34, lines 4-8, applicants' method is based on the discovery that increasing ATP within the phagolysosomes of APCs can stimulate the opening of ATP-sensitive pores in the phagolysosomes, thereby releasing the

phagocytosed antigen into the cytoplasm where it would be readily available for proteolytic processing and transport to the endoplasmic reticulum for association with MHC molecules. Thus, APCs primed according to the instant methods would be expected to provide enhanced presentation of the phagocytosed antigen and, consequently, a more robust T-cell stimulation compared to methods in the art. This result is confirmed by applicants' experimental data shown in Table I at page 35. Thus, applicants maintain that one of skill in the art would have a reasonable expectation of success in practicing the claimed methods. Moreover, given that the art teaches primed APC cells generally and their use to induce immunity in mammals, applicants maintain that no undue experimentation is required to practice this invention.

In view of the above remarks, applicants maintain that claims 1-32 satisfy the requirements of U.S.C. §112, first paragraph.

Summary

In view of the amendments and remarks made herein, applicants maintain that the claims pending in this application are in condition for allowance. Accordingly, allowance is respectfully requested.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

John P. White
Registration No. 28,678
Alan J. Morrison
Registration No. 37,399
Attorneys for Applicants
Cooper & Dunham, LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400

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Alan J. Morrison Date
Reg. No. 37,399